Conclusion: MBG underestimates MVO after an optimal revascularization in AMI compared to CMR. This study suggests the superior accuracy of delayed enhanced magnetic resonance (DEMR) over MBG for the assessment of myocardial reperfusion injury which is needed in clinical trials where the principal endpoint is the reduction of infarct size (IS) and MVO.

037

The relative contribution of the CYP2C19*2 polymorphism in the low responsiveness to clopidogrel in the VASP-02 study

Boris Aleil (1), Laurent Jacquemin (2), Fabien De Poli (3), Michel Zaehringer (1), Jean-Philippe Collet (4), Gilles Montalescot (4), Catherine Léon (5), Jean-Pierre Cazenave (5), Marie-Claude Dickele (3), Jean-Pierre Monassier (2), Christian Gachet (5)
(1) Clinique de l'Orangerie, Cardiologie, Strasbourg, France – (2) Hôpital Emile Muller, Service de Cardiologie, Mulhouse, France – (3) Centre Hospitalier Général, Service de Cardiologie, Haguenau, France – (4) Hôpital Pitié-Salpêtrière (AP-HP), Institut de Cardiologie and INSERM U856, Paris, France – (5) Institut National de la Santé et de la Recherche Médicale U.311, Etablissement Français du Sang – Alsace, Strasbourg, France

The CYP2C19*2 genetic variant is known to contribute to low responsiveness to clopidogrel treatment, leading to a higher rate of cardiovascular events. Systematic identification of the 2C19*2 carriers to predict the individual patient's response to clopidogrel is a matter of debate.

Data of the VASP-02 study comparing patients' responsiveness to 75 and 150 mg/day maintenance dose of clopidogrel (Aleil et al., J Am Coll Cardiol Intv 2008) were reanalyzed by determining the 2C19*2 carrier status of the patients. Platelet reactivity index (PRI) was determined using the VASP method. A PRI>69 % defines low responsiveness to clopidogrel.

In the 37 non responder patients, 42.4 % were 2C19*2 carriers versus 22.0 % in the responder patients (p=0.022). After multivariate analysis, 2C19*2 polymorphism and high body weight were two independent predictors of high PRI (odds ratio [95% confidence interval] 3.39 [1.06-10.84] p=0.039 and 3.14 [1.19-8.30] p=0.021) respectively. Increasing the maintenance dose of clopidogrel from 75 to 150 mg/day in non responder patients resulted in a significant decrease of PRI from 76.4±4.6 to 62.8±10.4 % (p<0.01) in 2C19*2 carriers and from 76.1±5.3 to 60.8±13.4 % (p<0.01) in non carriers. The mean decrease of PRI after doubling the dose was not significantly different between carriers and non carriers of the genetic variant (-13.6±9.3 and -15.3±11.8 % p=0.39, respectively).

CYP2C19*2 is an important determinant of the responsiveness to clopidogrel while other independent factors such as body weight also are involved. Hyporesponsiveness in 2C19*2 carriers can be easily overcome by doubling the maintenance dose of clopidogrel. Thus, combined functional pharmacodynamic monitoring and genetic determination of CYP profile should help improve patient's responsiveness to clopidogrel.

038

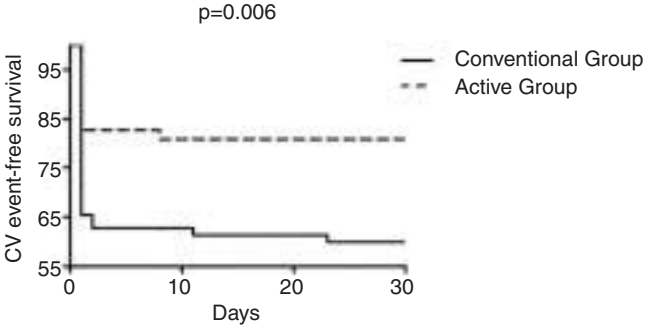
Glycoprotein IIbIIIa Inhibitors Improve Clinical Outcome after Coronary Stenting in Clopidogrel non Responders: a Prospective, Randomized Study

Thomas Cuisset (1), Corinne Frere (2), Jacques Quilici (3), Raphael Poyet (4), Laurent Bali (3), Pierre E Morange (2), Marie Christine Alessi (2), Jean Louis Bonnet (3)
(1) CHU Timone, Service de Cardiologie Interventionnelle, Marseille, France – (2) Inserm, U626, Faculté de Médecine Timone, Laboratory of Haematology, Marseille, France – (3) CHU Timone, Department of Cardiology, Marseille, France – (4) Inserm, U626, Faculté de Médecine, Laboratoire d'Hématologie, Marseille, France

Introduction: Numerous biological studies have reported inter-individual variability in platelet response to clopidogrel with clinical relevance. High Post treatment platelet reactivity (ADP-induced aggregation >70%) has been proposed to define Non response to clopidogrel. We assessed in clopidogrel non responders undergoing elective percutaneous coronary intervention (PCI) the benefit of adjusted antiplatelet therapy with glycoprotein IIbIIIa (GPIIbIIIa) antagonist administration during PCI for one month clinical outcome.

Methods and Results: 149 clopidogrel non-responders referred for elective PCI were prospectively included and randomized to "conventional group" (n=75) or "active group" with GPIIbIIIa antagonist (n=74). All patients received 250 mg aspirin and 600 mg clopidogrel before PCI and platelet testing. The rate of CV events at one month was significantly lower in the "active group" than in the "conventional group": 19% (n=14) vs. 40% (n=30), p=0.006, [OR (95%CI): 2.8(1.4-6.0)]. No patient in either group had post procedural TIMI major bleeding or required transfusions.

Conclusion: The present study suggested benefit of tailored antiplatelet therapy during elective PCI with GPIIbIIIa antagonist for clopidogrel non responders without increased bleeding risk.



039

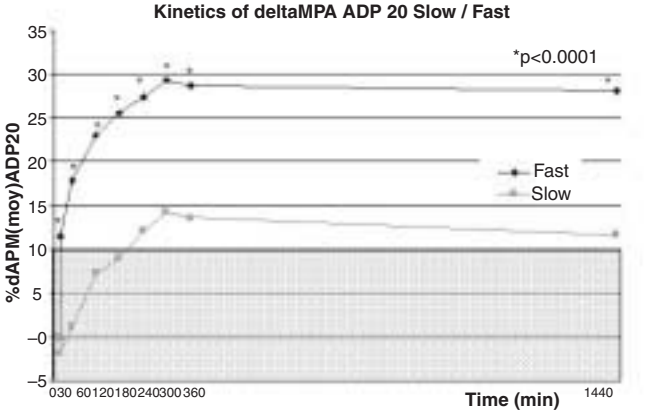
Slow Response to Clopidogrel Predicts Low Response

Anne Bellemain-Appaix, Gilles Montalescot, Johanne Silvain, Olivier Bathelemy, Farzin Beygui, Jean-Philippe Collet – Hopital Pitié Salpetrière, Cardiologie, Paris, France

Objectives: To determine if the speed of response to clopidogrel loading predicts the final degree of response to clopidogrel.

Background: Fast inhibition of platelet aggregation is important in the setting of ACS and PCI, but its relation to the final degree of inhibition is not well established.

Methods: We performed a post-hoc analysis of ALBION, which included 103 NSTE-ACS patients randomised to 300, 600 or 900mg LD of clopidogrel. Early kinetic profiles of ADP 20µmol/l Maximal Platelet Aggregation (MPA) and deltaMPA (with baseline sample as reference) were studied, with 8 time points within the 24 hours following loading. Low response was defined as deltaMPA<10%



Relationship between onset of action and magnitude

over the first 24 hours, fast response as deltaMPA≥10% within the first hour after loading (the others being slow responders), and high post-treatment platelet reactivity (HPPR) as MPA≥56.56% (fourth quartile). Inflammatory markers (PAC1 and P-selectin) and VASP were also evaluated according to onset of action.

Results: 55% of patients were slow responders. Non current smoking and BMI ≥ 25 kg/m_ were associated with slower and lower response. HPPR was more frequent in slow responders (28% vs 14% p<0.0001). There was a dose effect relationship on deltaMPA, with a trend for faster onset of platelet inhibition in the 900 mg LD group. Slow responders had slower and lower decrease of PAC1 and P-selectin, and higher VASPindex at 6 hours (76.5% vs 66.4%, p=0.019) and 24 hours (70.3% vs 61.5%, p=0.049).

Conclusions: Slow response to clopidogrel is a reliable marker of low response at 24 hours and HPPR. Whether early detection and correction of slow clopidogrel response is clinically relevant remains to be demonstrated.

040

Is it long-term (> 12 months) dual antiplatelet treatment necessary in diabetic patients treated with drug-eluting stents?

Vassilis Voudris, Panagiotis Karyofillis, Sophia Thomopoulou, Dennis V Cokkinos
Onassis Cardiac Surgery Center, Cardiology Dpt, Athens, Grèce

Background: Despite encouraging short-term results with drug-eluting stents (DES) in diabetes mellitus (DM) patients (pts) with coronary artery disease, the long-term safety is not clear. We investigated the influence of long-term (> 12 months) dual antiplatelet treatment (APLT) with aspirin and clopidogrel on clinical outcome in DM pts treated with DES.

Methods: The study included 552 consecutive DM pts (male 81%, mean age 65+9 years) that had been treated with DES and received dual APLT treatment for 12 months. Long-term clinical follow-up (FU) (mean time 30.4 + 11.6 months), obtained in 545/552 (99%) of them; 419 (77%) pts were on dual APLT (group A) and 126 (23%) on single APLT (group B). Major adverse cardiovascular event (MACE) on clinical FU was considered death (D), myocardial infarction (MI), percutaneous or surgical revascularization (REV), cerebrovascular accident (CVA), and hard end-points (HDP) was considered D, MI and CVA. Late stent thrombosis (LST) was defined as angiographic documentation of stent occlusion associated with an acute ischemic event, unexplained sudden D or MI not clearly attributable to another coronary lesion > 12 months post-procedure.

Results: Unstable angina at presentation was more frequent in group A pts (36% vs. 26%, p<0.05).The incidence of LST was 2.1% in group A and 0.8% in group B pts (p:ns); no difference was observed according to diabetic treatment (insulin vs. non-insulin dependent). At FU D was observed in 4.8% vs. 2.4%, MI 1.9% vs. 0.8%, and HDP in 8.4% vs. 4% between pts in group A and B respectively (p:ns). The rate of any REV and MACE was higher in pts in group A (20.3% vs. 6.3 %, and 26.7% vs. 11.1%, p<0.001); this difference was only observed in non-insulin-dependent pts. In a multivariate model ejection fraction <40% was predictor for LST (HR 14.5, 95% CI 3.9-49.4, p<0.001), and D/MI (HR 3.61, 95% CI 1.7-7.5, p=0.001), and multivessel disease for MACE (HR 2.0,95% CI 1.27-3.15, p=0.003).

Conclusion: Dual APLT > 12 months in DM pts treated with DES implantation is not associated with better clinical outcome or lower risk of LST.

041

Percutaneous coronary intervention of unprotected left main coronary artery for cardiogenic shock

Gilles Barone-Rochette, Gerald Vanzetto, Arnaud Fluttaz, Hélène Bouvaist, Stéphanie Marlière, Jacques Machecourt
CHU de Grenoble, unité de soins intensifs cardiologiques, Grenoble, France

Primary coronary angioplasty (PCA) of unprotected left main coronary artery (LM) in patients (pts) with cardiogenic shock (CS) is a high-risk procedure, carrying a high morbi-mortality.

Accordingly we aimed to assess the prevalence, clinical presentation, therapeutic workout and in-hospital and long-term prognosis of pts presenting with CS due to TIMI flow 0-1 LM thrombosis.

Over a 6-years period, and out of a prospective cath-lab database of 6062 files, 17 cases of CS secondary to LM thrombosis were identified and confirmed by reanalysis of angiograms. Therapeutic management and in-hospital outcome were obtained from medical files and prospective follow-up was obtained.

The study population consisted in 13 men (76%) with a mean age of 64±16 years, corresponding to a prevalence of 0.28 % of pts proposed for coronary procedure. Clinical presentation was an ACS with and without persistent ST-elevation in 11 (65%) and 6 cases (35%) respectively. Five patients (29%) received pre-hospital thromboysis, which failed to achieved reperfusion in all cases. Twelve patients (71%) undergone mechanical support (intra-aortic balloon pumping alone in 55%, extracorporeal life support alone in 5%, and both in 45%). The majority of PCA were performed with bare metal stent (n=14, 82%), under GPIIbIIIa antagonists in 8 cases, and instrumental thrombectomy in 3 cases. In-hospital death occurred in 5 pts (29%). At mean follow-up of 23 months (100% completed) survival rate was 53% for entire cohort and 75% among discharged pts. Most patients were in NYHA class I (7/9), with averaged left ventricular ejection fraction of 50+17%. One pts was implanted with a Thoratec device and is awaiting heart transplantation, and one is in terminal heart failure.

LM occlusion with CS has a very high mortality rate. However, PCA in such setting with use of aggressive mechanical life support carries an acceptable level of major adverse coronary event at medium and long-term prognosis.

042

Patients with recent history of ACS: frequency and characteristics of symptomatic and asymptomatic PAD in a French office based study (CALIPSO)

Nicolas Danchin (1), Pascal Priollet (2), Francois Dievart (3), Yves Cottin (4), Jean Ferriere (5), Serge Kownator (6), Marie Helene Barlet (7), George Pisica-Donose (7)
(1) Hôpital Européen Georges Pompidou, Paris, France – (2) Hôpital St Joseph, Paris, France – (3) Clinique Villette, Dunkerque, France – (4) Hôpital du Bocage, Dijon, France – (5) CHU Rangueil, Toulouse, France – (6) R Poincaré, Thionville, France – (7) BMS, Dépt. Médical Cardiovasculaire, Rueil Malmaison, France

Background: In ACS patients, presence of a peripheral arterial disease (PAD) or a low ankle brachial index (ABI) is associated with a higher CV risk in either symptomatic or asymptomatic PAD patients than ACS patients without PAD.

Objective: To determine the frequency and describe symptomatic and asymptomatic PAD patients, diagnosed by clinical examination and ABI measurement, in French population with recent history of ACS.

Methods: A 2-stage observational survey was conducted by 422 office-based cardiologists: 1) a registry part to provide a nationally representative overview and to estimate the prevalence of PAD and proportion of normal or low ABI in the overall.

2) a detailed part to asses and compare patients issued from registry with symptomatic or asymptomatic PAD and without PAD.

Results: 374 office based cardiologists recorded in the registry 2030 patients with a recent history of ACS and selected 1135 patients for the detailed part of the study.

Main characteristics of the registry patients were: mean age 66 years, 75% male, 30.3% STEMI, 22.7% NSTEMI and 47.1% UA. The prevalence of PAD in the registry population was 35.9% and between them 401 (55.1%) were symptomatic: intermittent claudication (321), history of angioplasty or bypass (221), amputations (12). Mean value of ABI measurement in the registry was 0.93 CI [0.92-0.94] with 32.3% less than 0.9.

In the detailed part of the study, the mean age was 65.7 years and 77.7% of patients were male. ACS characteristics: STEMI 32.1%, NSTEMI 22.4% and UA 45.5%. 624 patients were selected without PAD and 511 with PAD. Within these patients, 55.4% were symptomatic: intermittent claudication (20.3%), had a history of angioplasty or bypass (12.6%), or amputations (0.4%). Mean value of ABI for 1131 patients in the detailed study was 0.9 [0.89-0.91] and 42% had a low ABI (<0.9).

Conclusions: PAD is highly prevalent (35.9%) in patients with recent history of ACS and almost one half of these patients are asymptomatic.